PATENT COOPERATIC TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 04 October 2000 (04.10.00)	
International application No. PCT/US00/01205	**Applicant's or agent's file reference** PU3610WO
International filing date (day/month/year) 19 January 2000 (19.01.00)	**Priority date** (day/month/year) 19 January 1999 (19.01.99)
Applicant LENHARD, James, Martin	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

12 July 2000 (12.07.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer F. Baechler
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

US0001205

Form PCT/IB/331 (July 1992)

pdy 01/09/01 DPBS/ES/KC/File

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: DAVID J. LEVY
GLAXO WELLCOME, INC.
FIVE MOORE DRIVE
P.O. BOX 13398
RESEARCH TRIANGLE PARK, N.C. 27709-3398

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	03 JAN 2001
Applicant's or agent's file reference: PU3610WO	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US00/01205	19 JANUARY 2000	19 JANUARY 1999

Applicant: GLAXO GROUP LIMITED

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	J. S. Parkin
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1234

Form PCT/IPEA/416 (July 1992)★

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IPES/ES/1
EM

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PU3610WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/01205	International filing date *(day/month/year)* 19 JANUARY 2000	Priority date *(day/month/year)* 19 JANUARY 1999

International Patent Classification (IPC) or national classification and IPC
IPC(7): C12Q 1/00; C12N 15/00; G01N 33/00; A01K 67/00 and US Cl.: 435/4, 440; 800/3, 8

Applicant
GLAXO GROUP LIMITED

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I [X] Basis of the report

   II [ ] Priority

   III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV [ ] Lack of unity of invention

   V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [ ] Certain documents cited

   VII [ ] Certain defects in the international application

   VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12 JULY 2000	25 NOVEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer J. S. Parkin Telephone No. (703) 308-1234

COPIED TO

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/01205

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citati ns and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-70	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-70	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-70	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-34 and 41-54 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed screening methods. While reports of peripheral lipodystrophy, hyperlipidemia, and insulin resistance in conjunction with the administration of antiretroviral (ARV) combination therapies have been noted in the prior art, nevertheless, these reports fail to teach or suggest effective methods for ascertaining which ARVs are likely to adversely impact fat loss and/or redistribution. The prior art fails to teach or suggest screening methods having the precise claim limitations of the instant invention. For instance, screening methods employing the use of mesenchymal stem cells or preadipocytes and assaying for the specific biochemical activities claimed are not disclosed. The shortcomings of the prior art are further illustrated by the lack of availability of suitable animal models in which to predict the adverse consequences associated with ARV therapies.

Claims 35-40 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed screening method. Although the prior art discloses that PPAR/RXR receptor/ligand interactions play a role in adipogenesis, the precise effects of various ARVs on these binding interactions and its relevance to lipodystrophy or dyslipidemia *in vivo* remains to be elucidated. The need for such a screening methodology is further manifest by the various parameters that affect fat metabolism, often in an unpredictable manner. Thus, there is a need in the prior art for assays that detect the effects of ARVs on fat metabolism and provide results that can be directly extrapolated to the clinic.

Claims 55-61 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed transgenic animals and methods employing said animals. While the prior art discloses the preparation of transgenic animals that are useful for examining fat (Continued on Supplemental Sheet.)

Supplemental B x
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
metabolism, these animals contained single modifications that affect gene expression (i.e., overexpression of a desired gene product). However, the prior art fails to teach or suggest the preparation of transgenic animals, and methods of employing said animals, that express transgenes that confer ARV sensitivity to the animal. Thus, there is a clear need to develop a suitable animal model that will enable the skilled artisan to predict which ARVs will display adverse side-effects.

Claims 62-70 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed classification methods. As discussed *supra*, while reports of peripheral lipodystrophy, hyperlipidemia, and insulin resistance in conjunction with the administration of antiretroviral (ARV) combination therapies have been noted in the prior art, nevertheless, these reports fail to teach or suggest effective screening and classification methods that involve monitoring specific changes in gene expression.

———— NEW CITATIONS ————

NONE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

15

Applicant's or agent's file reference PU3610WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/01205	International filing date *(day/month/year)* 19 JANUARY 2000	Priority date *(day/month/year)* 19 JANUARY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/00; C12N 15/00; G01N 33/00; A01K 67/00 and US Cl.: 435/4, 440; 800/3, 8		
Applicant GLAXO GROUP LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I [X] Basis of the report

   II [ ] Priority

   III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV [ ] Lack of unity of invention

   V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [ ] Certain documents cited

   VII [ ] Certain defects in the international application

   VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12 JULY 2000	25 NOVEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer J. S. Parkin Telephone No. (703) 308-1234

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/01205

I. Basis f the rep rt

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-55 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 56-66 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-9 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/01205

V. R as ned statement under Articl 35(2) with regard t novelty, inv ntive step r industrial applicability; citati ns and explanati ns supp rting such statement

1. statement

Novelty (N)	Claims	1-70	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-70	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-70	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-34 and 41-54 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed screening methods. While reports of peripheral lipodystrophy, hyperlipidemia, and insulin resistance in conjunction with the administration of antiretroviral (ARV) combination therapies have been noted in the prior art, nevertheless, these reports fail to teach or suggest effective methods for ascertaining which ARVs are likely to adversely impact fat loss and/or redistribution. The prior art fails to teach or suggest screening methods having the precise claim limitations of the instant invention. For instance, screening methods employing the use of mesenchymal stem cells or preadipocytes and assaying for the specific biochemical activities claimed are not disclosed. The shortcomings of the prior art are further illustrated by the lack of availability of suitable animal models in which to predict the adverse consequences associated with ARV therapies.

Claims 35-40 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed screening method. Although the prior art discloses that PPAR/RXR receptor/ligand interactions play a role in adipogenesis, the precise effects of various ARVs on these binding interactions and its relevance to lipodystrophy or dyslipidemia *in vivo* remains to be elucidated. The need for such a screening methodology is further manifest by the various parameters that affect fat metabolism, often in an unpredictable manner. Thus, there is a need in the prior art for assays that detect the effects of ARVs on fat metabolism and provide results that can be directly extrapolated to the clinic.

Claims 55-61 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed transgenic animals and methods employing said animals. While the prior art discloses the preparation of transgenic animals that are useful for examining fat (Continued on Supplemental Sheet.)

Supplemental B x
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
metabolism, these animals contained single modifications that affect gene expression (i.e., overexpression of a desired gene product). However, the prior art fails to teach or suggest the preparation of transgenic animals, and methods of employing said animals, that express transgenes that confer ARV sensitivity to the animal. Thus, there is a clear need to develop a suitable animal model that will enable the skilled artisan to predict which ARVs will display adverse side-effects.

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---------- NEW CITATIONS ----------
NONE

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* PU3610WO

Box No. I TITLE OF INVENTION

METHODS OF SCREENING PROTEASE INHIBITORS, OF INDUCING MICE SUSCEPTIBLE TO HIV PROTEASE INHIBITOR-INDUCED DYSLIPIDEMIA, AND GENES ASSOCIATED THEREWITH

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

GLAXO GROUP LIMITED
Glaxo Wellcome House
Berkeley Avenue
Greenford, Middlesex UB6 ONN
GREAT BRITAIN

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

LENHARD, James Martin
900 Glenwood Avenue
Raleigh, NC 27605
United States of America

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: US

State *(that is, country)* of residence: US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Attn: LEVY, DAVID J.
GLAXO WELLCOME, INC.
Five Moore Drive
P. O. Box 13398
Research Triangle Park, NC 27709-3398
United States of America

Telephone No. 919-483-2370

Facsimile No. 919-483-7988

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked):*

Regional Patent

☒ **AP ARIPO Patent**: **GH** Ghana, **GM** Gambia, **KE** Kenya, **LS** Lesotho, **MW** Malawi, **SD** Sudan, **SL** Sierra Leone, **SZ** Swaziland, **UG** Uganda, **ZW** Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT

☒ **EA Eurasian Patent**: **AM** Armenia, **AZ** Azerbaijan, **BY** Belarus, **KG** Kyrgyzstan, **KZ** Kazakhstan, **MD** Republic of Moldova, **RU** Russian Federation, **TJ** Tajikistan, **TM** Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP European Patent**: **AT** Austria, **BE** Belgium, **CH and LI** Switzerland and Liechtenstein, **CY** Cyprus, **DE** Germany, **DK** Denmark, **ES** Spain, **FI** Finland, **FR** France, **GB** United Kingdom, **GR** Greece, **IE** Ireland, **IT** Italy, **LU** Luxembourg, **MC** Monaco, **NL** Netherlands, **PT** Portugal, **SE** Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ **OA OAPI Patent**: **BF** Burkina Faso, **BJ** Benin, **CF** Central African Republic, **CG** Congo, **CI** Cote d'Ivoire, **CM** Cameroon, **GA** Gabon, **GN** Guinea, **GW** Guinea-Bissau, **ML** Mali, **MR** Mauritania, **NE** Niger, **SN** Senegal, **TD** Chad, **TG** Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* Guinea-Bissau

National Patent *(if other kind of protection or treatment desired, specify on dotted line):*

☒ **AE** United Arab Emirates
☒ **AL** Albania
☒ **AM** Armenia
☒ **AT** Austria
☒ **AU** Australia
☒ **AZ** Azerbaijan
☒ **BA** Bosnia and Herzegovina
☒ **BB** Barbados
☒ **BG** Bulgaria
☒ **BR** Brazil
☒ **BY** Belarus
☒ **CA** Canada
☒ **CH and LI** Switzerland and Liechtenstein
☒ **CN** China
☒ **CU** Cuba
☒ **CZ** Czech Republic
☒ **DE** Germany
☒ **DK** Denmark
☒ **EE** Estonia
☒ **ES** Spain
☒ **FI** Finland
☒ **GB** United Kingdom
☒ **GD** Grenada
☒ **GE** Georgia
☒ **GH** Ghana
☒ **GM** Gambia
☒ **HR** Croatia
☒ **HU** Hungary
☒ **ID** Indonesia
☒ **IL** Israel
☒ **IN** India
☒ **IS** Iceland
☒ **JP** Japan
☒ **KE** Kenya
☒ **KG** Kyrgyzstan
☒ **KP** Democratic People's Republic of Korea
☒ **KR** Republic of Korea
☒ **KZ** Kazakhstan
☒ **LC** Saint Lucia
☒ **LK** Sri Lanka
☒ **LR** Liberia
☒ **LS** Lesotho
☒ **LT** Lithuania
☒ **LU** Luxembourg
☒ **LV** Latvia
☒ **MD** Republic of Moldova
☒ **MG** Madagascar
☒ **MK** The former Yugoslav Republic of Macedonia
☒ **MN** Mongolia
☒ **MW** Malawi
☒ **MX** Mexico
☒ **NO** Norway
☒ **NZ** New Zealand
☒ **PL** Poland
☒ **PT** Portugal
☒ **RO** Romania
☒ **RU** Russian Federation
☒ **SD** Sudan
☒ **SE** Sweden
☒ **SG** Singapore
☒ **SI** Slovenia
☒ **SK** Slovakia
☒ **SL** Sierra Leone
☒ **TJ** Tajikistan
☒ **TM** Turkmenistan
☒ **TR** Turkey
☒ **TT** Trinidad and Tobago
☒ **UA** Ukraine
☒ **UG** Uganda
☒ **US** United States of America CIP of U.S.S.N. 60/116,300; filed: Jan. 19, 1999 (19/01/99)
☒ **UZ** Uzbekistan
☒ **VN** Viet Nam
☒ **YU** Yugoslavia
☒ **ZA** South Africa
☒ **ZW** Zimbabwe

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

☒ DM Dominica
☒ CR Costa Rica

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)*

Supplemental Box *If the Supplemental Box is not used, this sheet need not be included in the request.*

*1. If, in any of the Boxes, **the space is insufficient** to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:*

*(i) **if more than two persons are involved as applicants and/or inventors** and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;*

*(ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication **"the States indicated in the Supplemental Box"** is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;*

*(iii) if, in Box No. II or in any of the sub-boxes of Box No. III, **the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America:** in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;*

*(iv) if, in addition to the agent(s) indicated in Box IV, there are **further agents**: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV:*

*(v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication **"patent of addition,"** or **"certificate of addition,"** or if, in Box No. V., the name of the United States of America is accompanied by an indication **"continuation"** or **"continuation-in-part"**: in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;*

*(vi) if, in Box No. VI, there are **more than three earlier applications whose priority is claimed:** in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;*

*(vii) if, in Box No. VI, the **earlier application is an ARIPO application:** in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.*

*2. If, with regard to the **precautionary designation statement** contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.*

*3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning **non-prejudicial disclosures or exceptions to lack of novelty**: in such case, write "Statement concerning non-prejudical disclosures or exceptions to lack of novelty" and furnish that statement below.*

Continuation of Box No. IV

PERRYMAN, David G.; KERBER, Lori L.; DADSWELL, Charles E.; GRASSLER, Frank P.; BRINK, Robert H.; RIEK, James P.; PRUS, Karen L.; SELBY, Elizabeth; MORGAN, Lorie Ann; BENNETT, Virginia C.; ROGERS, Christopher R.; DEPPENBROCK, Bonnie L.; and LEMANOWICZ, John L. all Glaxo Wellcome, Inc., Five Moore Drive, P. O. Box 13398, Research Triangle Park, N.C. 27709-3398, U.S.A.

HESKETH, Alan (GB); CRAWLEY, Karen (GB); DOLTON, Peter I. (GB); DAWSON, Hugh B. (GB); FILLER, Wendy Anne (GB); HACKETT, Ruth Elizabeth (GB); HAMMETT, Audrey G. C. (GB); LANE, Graham M. H. (GB); LEAROYD, Stephanie Anne (GB); QUILLIN, Helen Kaye (GB); REED, Michael A. (GB); REES, Marion (GB); STOTT, Michael John (GB); TEUTEN, Andrew J. (GB); THORNLEY, Rachel M. (GB) and VOLCKMAN, Janis Florence (GB) all in c/o Glaxo Wellcome plc., Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex, UB6 0NN, Great Britain

Continuation of Box No. V

TZ - Tanzania
MA - Morocco
US - Continuation-In-Part of U.S. Provisional Serial Nos.: 60/116,300; filed: January 19, 1999 (19/01/99); 60/137,620; Filed: June 04, 1999 (04/06/99); and 60/146,309; Filed: July 27, 1999 (07/27/99).

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 19 January 1999 19/01/99	60/116,300	US		
item (2) 04 June 1999 04/06/99	60/137,620	US		
item (3) 27 July 1999 27/07/99	60/146,309	US		

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1), (2), and (3)

** Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):*

ISA/ US

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*

Date *(day/month/year)* Number Country (or regional Office)

Box No. VIII CHECK LIST: LANGUAGE OF FILING

This international application contains the following **number of sheets:**

request	:	4
description (excluding sequence listing part)	:	55
claims	:	11
abstract	:	1
drawings	:	9
sequence listing part of description	:	
Total number of sheets	:	80

This international application is **accompanied** by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
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5. ☐ priority document(s) identified in Box No. VI as items(s):
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9. ☒ other *(specify):* CK$2,648.00; postcard; Cert. of Ex Mail# 348123347US

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

LORI L. KERBER

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1. Date of actual receipt of the purported international application:
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FEE CALCULATION SHEET

Annex to the Request

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International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference: **PU3610WO**

Applicant: **GLAXO GROUP LIMITED**

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . **240.00** T

2. SEARCH FEE . . . . . **700.00** S

International search to be carried out by **US**

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3. INTERNATIONAL FEE

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The international application contains **80** sheets.

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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A1

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60/146,309	27 July 1999 (27.07.99)	US

(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications

US	60/116,300 (CIP)
Filed on	19 January 1999 (19.01.99)
US	60/137,620 (CIP)
Filed on	4 June 1999 (04.06.99)
US	60/146,309 (CIP)
Filed on	27 July 1999 (27.07.99)

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(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: LENHARD, James, Martin [US/US]; 900 Glenwood Avenue, Raleigh, NC 27605 (US).

(74) Agents: LEVY, David, J.; Glaxo Wellcome, Inc., Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709–3398 (US) et al.

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

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(54) Title: METHODS OF SCREENING PROTEASE INHIBITORS, OF INDUCING MICE SUSCEPTIBLE TO HIV PROTEASE INHIBITOR–INDUCED DYSLIPIDEMIA, AND GENES ASSOCIATED THEREWITH

(57) Abstract

The present invention relates generally to the side effects caused by retroviral therapies, including protease inhibitors, nucleoside reverse transcriptase inhibitors, and non–nucleoside reverse transcriptase inhibitors. Specifically, the present invention provides methods of screening a protease inhibitor for its capacity to affect symptoms or clinical conditions associated with lipodystrophy or dyslipidemia and related metabolic disorders, such as metabolic syndrome X, obesity, cardiovascular disorders, and impaired glucose tolerance in diabetes, in a patient.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/01205

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) :C12Q 1/00; C12N 15/00; G01N 33/00; A01K 67/00
US CL :435/4, 440; 800/3, 8
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/4, 440; 800/3, 8

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

AIDSLINE, MEDLINE, USPATFUL, WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SHAW, A. J. et al. Disorders of fat distribution in HIV infection. International Journal of STD & AIDS. 1998, Vol. 9, pages 595-599, see entire document.	1-70
Y	CARR, A. et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. AIDS. 1998, Vol. 12, No. 7, pages F51-F58, see entire document.	1-70
Y	CARR, A. et al. Pathogenesis of HIV-1-protease inhibitor-associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance. Lancet. 20 June 1998, Vol. 351, pages 1881-1883, see entire document.	1-70

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
05 MAY 2000	25 MAY 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Jeffrey S. Parkin, Ph.D. Telephone No. (703) 308-1234

Form PCT/ISA/210 (second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/01205

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SHIMOMURA, I. et al. Insulin resistance and diabetes mellitus in transgenic mice expressing nuclear SREBP-1c in adipose tissue: model for congenital generalized lipodystrophy. Genes & Development. 1998, Vol. 12, pages 3182-3194, see entire document.	55-57